Diaspora Meeting 2006
Royal Academy of Medicine in Ireland - Neurology
Number 6 Kildare Street

Programme

THURSDAY, NOVEMBER 9TH

09.00—09.30 Registration and Coffee

Session 1
09.30 – 13.00

Round table discussion of presentation to Joint Oireachtas Committee Health and Children

The IICN welcomes representatives from:

- Neurological Alliance of Ireland
- Irish Society for Quality in Healthcare (Mr. Willie Reddy)
- Health Services Executive (Ms. Marie Lafoy, Ms. Deirdre Crowley, Ms. Antoinette Doosey

11.00-11.30 Tea and Coffee

13.00 – 14.15 Lunch
Session 2

Presentations for the Royal Academy of Medicine’s Registrar’s Prize in Neurology – Case Reports

14.15 Benign neuromyelitis optica over 18 years; relapsing paraproteinemic central demyelination
Lisa Costelloe, Michael Hutchinson.

Fitzpatrick AS, McDonnell G, Gray OM, McConville J

14.45 ‘I can’t remember, you’d better ask my wife!’
JA Johnston, C Lawthom and PEM Smith. University Hospital of Wales, Cardiff

15.00 Epstein Barr Virus Reactivation post Liver Transplantation: an unusual presentation.
Gorman G*, D’Arcy C, Professor McCormack**, Tubridy N*, Hutchinson M* Department of Neurology, St. Vincent’s University Hospital Elm Park, Dublin 4* Department of Gastroenterology/Liver transplantation, St Vincent’s University Hospital, Dublin 4**

15.15 Encephalopathy in a patient with familial hemiplegic migraine and mutation in ATP1A2 Gene.
A Merwick., D Fernandez, B McNamara, H Harrington.

15.30 Cerebral Ischaemia and Intracerebral Haemorrhage in Association with the Hypereosinophilic Syndrome
Sinead M Murphy 1, John P O’Dwyer 1, Philip Murphy 2, Joan T Moroney 1 Departments of Neurology 1 and Haematology 2, Beaumont Hospital, Dublin

15.45 – 16.15 Tea and Coffee

16.15 When Classical Migraine is Not Classical Migraine
Neligan A1, O’Riordan N1, Hurley HC2, O’Neill S2, Murphy G3, Ryder DQ3, Ryan A1 Departments of Neurology1, Vascular Surgery2 and Neuroradiology3, Cork University Hospital, Cork

16.30 L-2-hydroxyglutaric aciduria – a case report and review of the literature
O’Connor G (1), Hardiman O.(1), King M.(2), Salomons G.(3), Jackobs C.(3) (1) Dept. of Neurology, Beaumont Hospital, Dublin 9, Ireland (2) Dept. of Neurology, The Children's University Hospital, Dublin 1, Ireland
16.45 An unusual cause of visual loss.
Bradley D1, Birmingham N2, Keohane C2, Sweeney BJ1
Dept. of Neurology1, Dept. of Neuro-pathology2, Cork University Hospital,
Wilton, Cork.

17.00 Generating Hand Dysaesthesiae : The G.H.D. sign – straight to the diagnosis.
R Lonergan, M Alexander, C de Blacam, G Gorman, M Hutchinson, N Tubridy
Department of Neurology, St.Vincent’s University Hospital, Dublin 4

17.30 Announcement of winner of Registrar’s Prize - Case Report section.

The Institute appreciates the support of Janssen Cilag in sponsoring the Registrar’s Prize.
Irish Institute of Clinical Neuroscience

Diaspora Meeting 2006

Number 6 Kildare Street

Programme

FRIDAY, NOVEMBER 10TH

08.30 – 09.00 Tea and Coffee

Session 3

Presentation by IICN/Sanofi-Aventis Travel Award winners 2004 and 2005

09.15 Dr. Matt Greenway
Hypoxia-inducible factors in the pathogenesis of ALS.
Cecil B Day Laboratory, Mass General Institute for Neurodegenerative Diseases (MIND), Boston, USA.

09.45 Dr. Sherlyn Yeap
The search for an endophenotypic marker of schizophrenia: High-density electrophysiological studies.
Cognitive Neurophysiological Laboratory at The Nathan Kline Institute (NKI) for Psychiatric Research in New York.

10.15 – 10.45 Tea and Coffee

Session 4

Royal Academy of Medicine Registrar’s Prize in Neurology – Research Section

10.45Does the patient know best? : significant change in the Multiple Sclerosis Impact Scale (MSIS-29 physical) over four years.
Lisa Costelloe, Killian O’Rourke, Hugh Kearney, Christopher McGuigan, Leslie Daly, Niall Tubridy, Michael Hutchinson.

11.05 Paraoxonase promoter polymorphisms modify risk for sporadic ALS
Simon Cronin, Matthew J. Greenway, Sean Ennis, Andrew Green, Jochen H.M. Prehn and Orla Hardiman
The Irish ALS Research Group, Beaumont Hospital, Dublin.

11.25 Epilepsy Audit: Do we document everything?
Dr Mudassir Iqbal, Dr. Raymond Murphy, Neurology Dept, Tallaght Hospital, Dublin.

11.45 Patterns of routine EEG usage in a general adult ICU.
John C McHugh, MRCPI1,2, Therese Downey2, Raymond P Murphy FRCPI 1, Sean Connolly, FRCPI2.
1Department of Neurology, AMNCH, Tallaght, Dublin 24.  
2Department of Clinical Neurophysiology, AMNCH, Tallaght, Dublin 24.

12.05 Infarct volume and apraxia of speech in acute ischaemic hemispheral stroke
Sinead M Murphy, Colin P Doherty, Joan T Moroney
Departments of Neurology, Beaumont Hospital RCSI and St James’ Hospital

12.25 Impact of beta-interferon on accumulation of fixed disability in relapsing-remitting multiple sclerosis: a Bayesian analysis
O’Rourke K, Cathal Walsh, Michael Hutchinson
St. Vincent’s University Hospital, Dublin; Trinity College, Dublin

12.45 Moulding the sensory cortex: cortical sensory discrimination improves with botulinum toxin injection for cervical dystonia
Walsh R, Michael Hutchinson
St. Vincent’s University Hospital, Elm Park, Dublin 4, Ireland

13.05 Neurophysiological, histological, and measured strength potentials of “clinically unaffected” muscles in post polio syndrome (PPS).
Gorman G., Cahalane E., Lynch C., Farrell M., Connolly S., Hardiman O.
Department of Neurophysiology, St. Vincent’s University Hospital, Elm Park,
Department of Pathology, Beaumont Hospital, and Department of Neurology,
Beaumont Hospital, Dublin, Ireland.

13.30 Announcement and presentation of Award Registrar’s Prize in Neurology – Research

The Institute appreciates the support of Janssen Cilag in sponsoring the Registrar’s Prize.

13.15 – 14.15 Lunch

Session 5

Diaspora Presentations

14.15 Audit of a Novel Multi Disciplinary Goal Setting Process in a Regional Rehabilitation Unit
The Regional Neurological Rehabilitation Unit (RNRU) at Homerton University Hospital NHS Foundation Trust, Homerton Row, London, E9 6SR.
14.40 IL-17 producing T cells and their induction in Multiple Sclerosis
JM Fletcher\textsuperscript{1,2}, L Costelloe\textsuperscript{2}, C O’Farrelly\textsuperscript{3}, N Tubridy\textsuperscript{2} and KHG Mills$^1$
\textsuperscript{1} Trinity College Dublin
\textsuperscript{2} St Vincent’s University Hospital
\textsuperscript{3} University College Dublin

15.05 Assessment of the impact and value of continuous video-EEG monitoring on clinical management and patient outcome.
Ronan Kilbride MB MRCPI
Epilepsy Service, VBK 830 Department of Neurology Massachusetts General Hospital, Boston, U.S.A.

15.30 A multicentre study of BRD2 as a risk factor for juvenile myoclonic epilepsy.
John M Lynch MRCPI, Gianpiero L. Cavalleri PhD, Nicole M. Walley BS, Nicole Soranzo PhD, John Mulley Ph.D, Colin P. Doherty MD, Ashish Kapoor MSc, Chantal Depondt MD, Ingrid E Scheffer MBBS PhD FRACP, Armin Heils MD, Anne Gehrmann BS, Peter Kinirons MRCPI, Sonia Gandhi MRCP, Parthasarathy Satishchandra D.M Neuro, FANS, Nicholas W. Wood FRCP, PhD, Anuranjan Anand PhD, Thomas Sander MD, Samuel F Berkovic MDBS FRACP, Norman Delanty, David B. Goldstein PhD., Sanjay M. Sisodiya FRCP, PhD. Depts of Clinical and Experimental Epilepsy, and Molecular Neuroscience, Institute of Neurology, University College London, UK

15.55 Tea and Coffee

16.15 An Uncommon Peroneal Nerve Palsy
Martin Rutledge
Neurology SpR, Guy’s & St. Thomas’ Hospitals, London

Bryan Traynor

17.05 Interferon-Inducible Blood Gene Expression in Dermatomyositis is Specific and Reflects Disease Activity.
Ronan J Walsh, MB, MRCPI, FRCPC (Neurology), Instructor in Neurology, Harvard Medical School, Brigham and Women's Hospital, Boston, USA

17.30 The Epilepsy Phenome Genome Project (EPGP)
Peter Widdess-Walsh
The Institute of Neurology at St. Barnabas Medical Center, New York University Medical Center, Epilepsy Phenome Genome Project Consortium
Benign neuromyelitis optica over 18 years; relapsing paraproteinemic central demyelination

Lisa Costelloe, Michael Hutchinson.

Background
Neuromyelitis optica (NMO) is a disabling demyelinating disease associated with antibodies to aquaporin-4 in 70% of patients. We describe a patient with a benign NMO for 18 years associated with an IgM kappa paraproteinaemia; disabling relapses responded well to steroids.

History
In 1988, our patient developed retrobulbar neuritis at the age of 43. Over the next 18 years he had six demyelinating episodes; four being longitudinally extensive cord lesions, and two large areas of demyelination in the pons and midbrain responding well to steroids. Current functional deficit consists of a blind left eye, mild gait ataxia, a neurogenic bladder, and erectile dysfunction. He continues to regularly play 18 holes of golf. Repeated MRI brain has revealed no cerebral hemisphere involvement. CSF examination between relapses showed no white cells, oligoclonal bands were negative and IgG index was normal. In 2000, a serum monoclonal IgM kappa band was detected. Urine immunofixation, β2-microglobulin, and skeletal survey were normal. Bone marrow aspirate showed 7% plasma cells. NMO IgG testing was negative on two occasions. He has remained relapse free since commencing a course of Rituximab treatment.

Discussion
Our patient has the clinical phenotype of antibody-negative NMO with an unusually benign, and exquisitely steroid responsive course. There is a concomitant monoclonal gammopathy of undetermined significance in the serum. We postulate that this monoclonal band contains an antibody to the aquaporin-4 water channel resulting in CNS demyelination analogous to the peripheral demyelinating neuropathy associated with paraproteinemia.
Opsoclonus Myoclonus Syndrome associated with Benign Ovarian Teratoma.  
A case report and literature review.

Fitzpatrick AS, McDonnell G, Gray OM, McConville J

Background
The Opsoclonus Myoclonus Syndrome (OMS) is characterised by nonrhythmic involuntary ocular oscillations, axial and segmentary myoclonia and cerebellar ataxia. It can be a post-infectious, paraneoplastic or idiopathic phenomenon; most commonly associated with neuroblastoma in children and lung or ovarian malignancies in adults.

Case report
We report the case of a fifteen-year-old girl who presented with subacute onset of opsoclonus and myoclonus, ataxia, nausea and vomiting. Investigation out ruled infection, neuroblastoma, chest and breast malignancy but revealed a right-sided benign ovarian teratoma. Anti-neuronal antibodies were negative. The patient was treated with clonazepam, immunomodulatory treatment including intravenous steroids and immunoglobulin but showed the most improvement in response to surgical removal of the teratoma.

Discussion
In the light of significant clinical improvement in response to tumour removal we discuss OMS as a paraneoplastic manifestation of benign ovarian teratoma. Case reports have suggested a variety of neurological paraneoplastic manifestations of this type of tumour but its association with OMS have not previously been described.
‘I can’t remember, you’d better ask my wife!’

University Hospital of Wales, Cardiff
JA Johnston, C Lawthom and PEM Smith

In general medicine, general neurology and in epilepsy clinics the complaint of short-term memory loss by individuals and their relatives is commonplace. In the absence of a neurodegenerative disorder, psychological, pharmacological and other co-morbidities are usually to blame and we as physicians often have little to offer in terms of treatment. However recent developments in antibody-mediated encephalitis sheds light on potentially immunoresponsive conditions that present with subacute amnesia.

In light of this, a 65 year old man who presented after 4 generalised-tonic-clonic seizures and short-term memory loss was found to have significantly elevated voltage-gated potassium channel antibodies (KCVG) in a titre of 2838 (normal range < 100), bilateral hippocampal high signal on MRI, right ictal discharges on EEG, dysautonomia, hyponatraemia and despite the absence of neuromyotonia and without an underlying malignancy, yielded a potentially treatable diagnosis, of non-paraneoplastic potassium channel antibody mediated encephalitis. Clinical management is going and has taken the form of immunosuppression with immunoglobulins and steroids.

This case demonstrates that KCVG antibody mediated encephalitis is easily diagnosable by serological testing and as a diagnosis is certainly overlooked, potentially reversible and should form part of our diagnostic repertoire in the patient that presents with seizures, cognitive decline and amnesia.
Epstein Barr Virus Reactivation post Liver Transplantation: an unusual presentation.

Gorman G*, D’Arcy C, Professor McCormack**, Tubridy N*, Hutchinson M*
Department of Neurology, St. Vincent’s University Hospital Elm Park, Dublin 4*
Department of Gastroenterology/Liver transplantation, St Vincent’s University Hospital, Dublin 4**

Abstract
A 59-year-old, right-handed woman presented with a seven day history of gradual onset of blurred vision of her right eye. She denied any other neurological symptomatology. She had undergone orthotopic liver transplantation fifteen months prior secondary to non A non B fulminant liver failure.

Clinical examination revealed her to be alert and orientated, with bilateral pale swollen discs with haemorrhages on fundoscopy. Initial investigations including Magnetic Resonance Imaging (MRI) with gadolinium, venography, pituitary and orbital nerve views revealed non specific high signal changes within the white matter consistent with ischaemia and increased signal uptake in the left optic nerve only. Repeated lumbar puncture revealed increased opening pressure with associated pleocytosis. Immunophenotyping of the lymphocytes showed proliferation of T cells with non clonal B cells. CSF was positive for Epstein Barr virus (EBV) DNA. Concomitant whole blood was positive for EBV IgM suggesting active EBV disease.

The working diagnosis was post transplant lymphoproliferative disease (PTLD). Her immunosuppression was reduced and she was commenced on dexamethasone.

PTLD is the most common non cutaneous malignancy in solid organ transplant recipients with significant morbidity and mortality. CNS involvement is associated with a poorer outcome. Most PTLD is driven by EBV infection which promotes oncogenic activation. Extra nodal disease is common and presentation is often non specific delaying diagnosis.
Encephalopathy in a patient with familial hemiplegic migraine and mutation in ATP1A2 Gene.

A Merwick., D Fernandez, B McNamara, H Harrington.

33 year old female with a history of migraine presented with acute confusional state, dysphasia and right lower limb paresis, preceded by headache. Symptoms evolved over 12 hours. On initial assessment the patient was orientated in person, but not in place or time. She became increasingly agitated with falling level of consciousness and was transferred to the care of the neurology service. Speech became incomprehensible with localisation to pain was the best motor response. The patient made a full recovery over 5 days.

The patient had a known family history of migraine, and family members had been previously seen at specialist headache clinic.

Investigations
MRI brain and MR angiogram normal. EEG showed left sided focal slowing. lumbar puncture no white cells, CSF protein 0.35g/l, glucose 4.7 mml/l. Herpes simplex virus PCR negative.

Further family history was elicited. The patient’s father had been admitted to a psychiatric ward for 7 days with a similar episode. By linkage analysis, linkage to chromosome 1q23 had been demonstrated previously. Genetic testing in the family showed a novel ATP1A2 gene mutation, with detection of a G-C substitution in exon 22. This mutation results in replacement of aspartic acid residue with histadine at position 999 in Na+k+ATPase protein (D999H).

Conclusion
In patients who present with features of encephalopathy, history of migraine should be elicited. This case is the first documented case of migraine associated encephalopathy in a patient with a D999H mutation in the ATP1A2 gene seen in familial hemiplegic migraine.
Cerebral Ischaemia and Intracerebral Haemorrhage in Association With the Hypereosinophilic Syndrome.

Sinead M Murphy¹, John P O’Dwyer¹, Philip Murphy², Joan T Moroney¹
Departments of Neurology¹ and Haematology², Beaumont Hospital, Dublin

The hypereosinophilic Syndrome (HES) is a rare group of disorders characterised by overproduction of eosinophils and evidence of organ damage. Ischaemic stroke has been reported in this condition due to cardioembolism; anticoagulation has been used on this basis. Intracerebral haemorrhage (ICH) or intracerebral vasculopathy have not been reported in the HES.

A 44-year-old man presented with two right hemispheric TIAs, followed 10 days later by a large right-sided ICH. Full blood count showed persistently raised eosinophils, peak 12.18 x10⁹/L (normal 0.04-0.4 x10⁹/L). He was commenced on steroids because of neurological deterioration, with rapid improvement in mental status and eosinophil count. Investigations subsequently confirmed HES. He was commenced on a tyrosine-kinase inhibitor, which has been reported of benefit in HES. He improved clinically and blood count showed marginally raised eosinophils of 0.44 x10⁹/L four months later.

The recurrent right hemispherical localisation of symptoms suggested fixed intracranial arterial pathology. The other novel feature of our case was the occurrence of ICH. Our patient’s clinical presentation, investigations and dramatic response to steroids support an inflammatory vasculopathy as the underlying stroke mechanism. Thus careful consideration of alternative stroke mechanisms in patients with HES is important to guide selection of appropriate stroke therapy.
When Classical Migraine is Not Classical Migraine.

Neligan A, O’Riordan N, Hurley HC, O’Neill S, Murphy G, Ryder DQ, Ryan A. Departments of Neurology, Vascular Surgery and Neuroradiology, Cork University Hospital, Cork

Case
A 48-year-old lady presented to A&E with headache and visual disturbance 5 days following a road traffic accident. She represented 2 days later with headache and transient dysarthria. Neurological examination and CT brain were normal. Past history included migraine with visual aura, hypertension and hyperthyroidism. Her headaches and visual symptoms since the accident were similar to previous migraines but more frequent and severe. Diagnosis at this stage was felt to be post-traumatic headaches or recurrence of her migraine.

Results
MRI Brain showed some non-specific white matter changes. Carotid doppler ultrasound showed markedly reduced flow velocities in the internal carotids bilaterally. MR angiogram of neck vessels showed bilateral complete occlusion of the extracranial internal carotids. A diagnosis of spontaneous traumatic carotid artery dissection was considered. Subsequent 4-vessel angiography however showed diffuse concentric narrowing with almost complete occlusion of both internal carotids. Collateral supply was provided by external carotids via maxillary and ophthalmic arteries in addition to the posterior circulation. On the left internal carotid there was definite abnormality suggestive of beading Renal angiography on the left side showed beading pathognomonic of fibromuscular dysplasia (FMD).

Conclusion
Although difficult to demonstrate because of diffuse concentric narrowing, it is likely that traumatic dissection completed occlusion of internal carotids already chronically narrowed by longstanding fibrodysplastic change. Craniocervical dissection is a recognised complication of FMD. This case however is distinctly unusual in that there was no neurological deficit despite complete occlusion of the anterior circulation and the only persistent symptom was of “migrainous headache”.
L-2-hydroxyglutaric aciduria – a case report and review of the literature

O’Connor G.(1), Hardiman O.(1), King M.(2), Salomons G.(3), Jackobs C.(3)
(1) Dept. of Neurology, Beaumont Hospital, Dublin 9, Ireland
(2) Dept. of Neurology, The Children’s University Hospital, Dublin 1, Ireland
(3) Dept. of Paediatrics (Metabolic Unit), University Hospital VU, Amsterdam, the Netherlands

We report the case of a 26-year-old man who was referred to our service after a fall with a prolonged loss of consciousness and a very slow recovery. He had first been assessed by our service at the age of 16, for management of epilepsy, and had been noted by his family to have a gradual deterioration in gait, speech, co-ordination and intellectual ability over the intervening years. Examination on this admission revealed mental deficiency, evidence of cerebellar dysfunction, brisk deep tendon reflexes, bilateral ptosis and bilateral up-going plantar responses. He was also noted to be macrocephalic. MRI imaging revealed extensive signal abnormality in both cerebral hemispheres, consistent with hypomyelination. Screening for a metabolic cause revealed an elevated urinary L-2-hydroxyglutaric acid level (1354 mmol/mol creat, normal range 1.3 – 18.9). Genetic analysis revealed the presence of a mutation in the gene locus 14q22.1 which has not been previously described in this condition, a C>G transversion in exon 7. On the basis of the biochemical and imaging results, a diagnosis of L-2-hydroxyglutaric aciduria was made – the first such case reported in Ireland. We review the available literature on this rare disease, in terms of clinical presentation, imaging findings, and pathogenesis.
An unusual cause of visual loss.

Bradley D1, Birmingham N2, Keohane C2, Sweeney BJ1
Dept. of Neurology1, Dept. of Neuro-pathology2, Cork University Hospital, Wilton, Cork.

Case
A 23yo lady presented in 2005 with a sudden severe left-sided visual loss. She described a 2 year history of blurred vision, commencing six weeks after a normal pregnancy. Examination revealed a relative afferent papillary defect, a pale optic disc, and chorioretinitis with cotton wool spots and red spots. She subsequently had sudden visual loss in the right eye while receiving IV steroid treatment. She was treated with IV cyclophosphamide with no recovery of vision.

Investigation
MRI revealed areas of non-enhancing high signal intensity in the occipital regions. VEP studies showed poorly formed responses. Immunoglobulin levels were elevated and there were oligoclonal bands in the CSF. Mitochondrial disease screening was negative as was serum/CSF lactate and a vasculitic screen. PCR revealed HLA-B07. Brain biopsy showed occluded hyalinised vessels in the parenchyma with secondary white matter degeneration, interpreted as ischaemic. This was compatible with the clinical suspicion of Neuro-Bechet syndrome.

Discussion
Bechet’s Syndrome is an idiopathic vasculitic condition. The recommended diagnostic criteria are recurrent oral ulceration plus two of the following: skin lesions, genital lesions, ocular lesions or skin pathergy. Neurological involvement is uncommon. Clinical features are diverse including, for example, headache, confusion, cerebellar and brainstem syndromes, or ophthalmoplegia, among many others. There is a high morbidity with fifty percent having moderate to severe disability at 10 years. Histopathological findings are non-specific and usually include lymphocytic vasculitis among a range of other findings. Exclusion of differential diagnoses is possible, including amyloid or CADASIL.

R Lonergan, M Alexander, C de Blacan, G Gorman, M Hutchinson, N Tubridy
Department of Neurology, St. Vincent’s University Hospital, Dublin 4

Introduction
The increasing popularity of hair-straightening devices such as the G.H.D. (‘Good Hair Day’, the trade name now a widely accepted acronym for hair straighteners) in daily lives of many young women has assumed clinical relevance.

Case 1
A 21 year old right-handed woman described symptoms of left arm claudication precipitated by sustained shoulder abduction whilst straightening her hair at weekends. Upper limb pulses were impalpable and carotid pulses asymmetrical. CT Pulmonary angiogram demonstrated multiple stenoses of the ascending aorta, left subclavian and left internal carotid arteries. Takayasu’s arteritis was diagnosed and steroid therapy commenced.

Case 2
Similarly, a 32 year old right-handed woman described arm claudication symptoms whilst straightening her hair, progressing over a six month period. The Adson and Elevated Arm Stress Test were positive. CT Angiogram and formal angiography confirmed subclavian stenosis due to a right-sided axillary fibrous band, and a left-sided cervical rib was seen on chest X-ray.

Conclusion
Claudication and neurological symptoms induced by thoracic outlet obstruction and vascular pathology may be identified on concise history taking. Exacerbation of symptoms during hedge-clipping and painting, once described as classical symptoms of TOS, are now less frequently encountered in practice. Therefore, we propose the G.H.D. sign as a useful screening tool in young patients in whom upper limb claudication is suspected.